Remarks

Applicant's counsel thanks the Examiner for the careful consideration given the application.

Claim Rejections – 35 USC § 112

Claims 36, 51-54 and 58 have been amended to overcome the rejections set forth in part 3. of the Office Action. It is believed that the amendments obviate the rejections.

Claim Rejections – 35 USC § 102

Talmor '181

Claim 32 has been rejected as being anticipated by Talmor '181. This rejection is respectfully contended for the following reasons.

Firstly, claim 32 requires that the skin tissue from which electromagnetic fluorescent radiation is measured is clinically healthy, intact skin tissue of which an autofluorescence value is determined.

According to Talmor '181, skin tissue has been subjected to a PDT treatment based on a systemic or topical application of a tumor-localizing photosensitizing agent, which after illumination and excitation with light in the presence of oxygen, gives rise to highly reactive and cytotoxic single molecular oxygen which causes tumor regression. During PDT treatment, light should be applied to the tumor until the photosensitizer agent is consumed by the beneficial chemical reaction. Once this reaction is complete and the agent is consumed, any additional light applied to the tumor may have little value. The presence of the photosensitizing agent is determined by analyzing the spectrum of the light emitted by the photosensitizing agent present in the skin (col. 1, l. 37-49).

Another application disclosed in Talmor '181 is photo dynamic diagnostics (PDD). In this application, detection of a chemical in the tissue is used for tumor diagnosis, since chemical concentrations in the tumor are much higher than in healthy tissue. The chemicals are detected by measuring the chemical fluorescence. (col. 2, l. 9-20).

Thus, according to Talmor '181, the fluorescent radiation is the fluorescence of a chemical that has been applied to a skin suffering from cancer, which skin has been treated with a photosensitizer agent, and not the autofluorescence of clinically healthy, intact skin tissue (i.e. skin tissue known to be clinically healthy and intact) as is required by claim 32.

Secondly, claim 32 requires that an amount of fluorescent radiation is received and measured and that a signal is generated in response to the measured amount of fluorescent radiation, the surface area of the skin from which the measured fluorescent radiation is received having a size of at least 1 cm^2.

Talmor '181 discloses an apparatus for monitoring an image of a treatment site and for measuring spectral emissions from a portion of that region.

According to Talmor '181, col. 5, l. 66 – col. 6, l. 16, a small spot or shadow will appear in each camera image at the point where light guide 24 (Fig. 2) connected to spectrometer 20 is coupled to window 30 (Fig. 2). Alternatively, in an embodiment where the light guide is not coupled to the window, such as that shown in Figs. 3 or 4, a computer generated mark may be transmitted to the display to appear in each image at the place where the spectrometer measured the spectrum. Camera 18 preferably displays a larger portion of the treatment site than is sensed by spectrometer 20. In this manner, the operator while watching the display can view a large portion of treatment site 16, pan housing 12 about the treatment site, and clearly identify various portions of affected region 48 of treatment site 16 and their corresponding spectral behavior.

The camera does not generate a signal which represents a fluorescence value measured from a surface area of the skin of at least 1 cm^2, but rather generates signals representing amounts of light received from much smaller skin surface portions at which corresponding pixels of the CCD camera are focused. It is irrelevant that the detector 18 receives light from an image area larger than 1 cm^2, since the detector 18 does not generate a signal which represents a fluorescence value measured from the whole image area.

In contrast to the camera, the spectrometer 20 does generate a signal which represents a fluorescence value measured from a surface area. An image of the treatment site (obtained using detector 18) and the spectral measurement of the treatment site can be measured at the same time. The light guide preferably receives light emitted from a spot on the treatment site measuring between 1 and 10 mm^2 (Talmor '181, col. 4, l. 29-31, col. 5, l. 4-8 and l. 29-43). This is clearly smaller than a surface area of the skin of at least 1 cm^2 as is required by claim 32.

Accordingly, claim 32 is not anticipated by Talmor '181 because the irradiated skin of which the fluorescence is measured is not clinically healthy skin of which an autofluorescence value is determined and because the measured amount of fluorescence is received from a surface area smaller than 1 cm^2.

Essentially the same arguments apply to claim 47, which requires circuitry for generating an autofluorescence value for the clinically healthy, skin tissue in agreement with a the measured amount of fluorescent radiation and requires the fluorescent radiation detector to be arranged for measuring the amount of electromagnetic fluorescent radiation received from a surface of the skin tissue behind the radiation window having a size of at least 1 cm^2. Accordingly, also claim 47 is not anticipated by Talmor '181.

The same arguments also apply to claims 62 and 66, except that claims 62 and 66 require that the measured fluorescent radiation is received from a surface area of the skin larger than 0.1 cm^2 (instead of at least 1 cm^2 as defined in claims 1 and 47).

According to Talmor '181, the light guide preferably receives light emitted from a spot on the treatment site measuring between 1 and 10 mm^2. This is smaller than "larger than 0.1 cm^2" as is required by claims 62 and 66. Accordingly, also claims 62 and 66 are not anticipated by Talmor '181.

Kollias et al. '059

Kollias et al. '059 discloses measuring glucose concentrations by using fluorescence. Figs. 10A and 10B, schematically disclose incoming light λ_i entering the skin via a first surface portion of the skin and outcoming light λ_o which is received from a second surface portion next to the first surface portion via which the incoming light enters the skin.

Claim 32 requires that an amount of fluorescent radiation is received and measured and that a signal is generated in response to the measured amount of fluorescent radiation, the measured fluorescent radiation being received from a surface area of the skin of at least 1 cm^2.

According to Kollias et al. '059, the irradiated skin surface may be less than about 1 square cm and is more preferably about 0.2 square cm. Kollias et al. does not disclose the size of the skin surface area from which the measured amount of radiation is received. Fig. 2 and even Figs. 10A and 10B are only of a very schematic nature and therefore do not disclose the size of the surface from which the fluorescent radiation is received. In as far as Figs. 10A and 10B, disclose anything with respect to the size of the surface from which the radiation is received, these drawings do clearly not disclose that the size of the skin surface from which the fluorescent radiation is received is larger than the irradiated skin surface area. Thus, Kollias et al. '059 does not disclose that the size of the skin surface from which the fluorescent radiation is received is at least 1 cm^2. Therefore claim 32 is not anticipated by Kollias et al. '059.

Essentially the same arguments apply to claim 47, which requires the fluorescent radiation detector to be arranged for measuring the amount of fluorescent radiation received from a surface having a size of at least 1 cm^2.

The same arguments also apply to claims 62 and 66, except that claims 62 and 66 require that the measured fluorescent radiation is received from a surface area of the skin larger than 0.1 cm^2 (instead of at least 1 cm^2 as defined in claims 1 and 47). As observed above, the surface sizes of 0.2 cm^2 and about 1 cm^2 are only disclosed in Kollias et al. '059 as sizes of the irradiated surface and not as sizes of the surface from which radiation emitted by the skin is received.

Moreover, claims 62 and 66 each require that the measured fluorescent radiation is received from a portion of the irradiated surface portion of the skin only.

Kollias et al. '059 only discloses that the measured fluorescent radiation is received from a surface portion of the skin next to the irradiated surface portion of the skin (see Figs. 10A and 10B). Thus, Kollias et al. '059 does also not disclose the feature of claims 62 and 66 that the measured fluorescent radiation is received from a portion of the irradiated surface portion of the skin only.

It is therefore concluded that Kollias et al. '059 does not anticipate any of the claims 32, 47, 62 and 66.

Anderson et al. '127

Anderson et al. '127 discloses methods and systems for treating inflammatory, proliferative skin disorders, such as psoriasis, with ultraviolet phototherapy. The methods and systems use optical techniques to scan a patient's skin, designate areas of affected skin, and selectively deliver high doses of phototherapeutic ultraviolet radiation to the designated areas. To insure that only affected areas of skin are designated for the high doses of UV radiation, the methods and systems use one or more optical diagnostics that relate to independent physiological features of affected skin.

Claim 32 requires that an amount of fluorescent radiation is received and measured and that a signal is generated in response to the measured amount of fluorescent radiation, the measured fluorescent radiation being received from a surface area of the skin of at least 1 cm^2.

Anderson et al. '127 does disclose that selected areas may be less than about 1 cm^2 (Anderson et al. '127, col. 3, l. 11-12). However, this passage does not relate to the size of the surface from which a measured amount of fluorescence is simultaneously received, but to the size of the area from which radiation is detected and which is selected to be exposed to phototherapeutic radiation e.g. from a laser (Anderson et al. '127, col. 3, l. 3-11). The UV beam, which is used for both irradiating the skin to cause excitation resulting in fluorescence and therapeutic treatment of the psoriasis, is scanned over the skin. More specifically, the optical diagnostics may for instance scan a selected area (Anderson et al. '127, col. 6, l. 49-50). Since the UV beam scans over the selected area, it cannot be derived from the size of the selected area what is the size of the skin surface from which the measured amount of fluorescence is simultaneously received.

Anderson et al. '127 further discloses that the surface that is simultaneously irradiated is a spot having a size of less than about 1 cm and typically about 1 to 4 mm (Anderson et al. '127, col. 10, l. 33-37) and that a lens 50 is positioned to couple only fluorescence and reflectance

from the area of the skin coincident with treatment beam 40 into fiber 48 (Anderson et al. '127, col. 11, l. 45-48). Thus, the size of the spot from which radiation is simultaneously received is not at least 1 cm^2 as is required by claim 32.

Therefore claim 32 is also not anticipated by Anderson et al. '127.

Essentially the same arguments apply to claim 47, which requires the fluorescent radiation detector to be arranged for measuring the amount of fluorescent radiation received from a surface having a size of at least 1 cm^2.

Claims 62 and 66 require that the measured fluorescent radiation is received from a portion of the irradiated surface portion of the skin only. As discussed above, Anderson et al. '127 only discloses that a lens 50 is positioned to couple only fluorescence and reflectance from the area of the skin coincident with treatment beam 40 into fiber 48 (Anderson et al. '127, col. 11, l. 45-48) and not that the lens is arranged for coupling only fluorescence and reflectance from a portion of the area of the skin coincident with treatment beam 40 into fiber 48. Accordingly, also claims 62 and 66 are not anticipated by Anderson et al. '127.

Observations – 35 USC § 103

With respect to claims 32 and 47, it is observed that none of the cited documents discloses to provide that the size of the skin surface from which the measured fluorescent radiation is received is at least 1 cm^2. Accordingly, it would not have been obvious for the skilled person to provide such a solution to obtain an accurate yet easily performable measurement of very low levels of average autofluorescence without exposing the skin to levels of excitation radiation that cause discomfort in the form of heat and/or sunburn. By simultaneously measuring over a large surface area, very low levels of average autofluorescence of clinically healthy skin can be measured and the easily obtainable results can be used as an indication of the AGE content, which may, in turn, be used as an early indicator of diabetes mellitus and other conditions indicating an increased risk of cardiovascular complications. For instance, when set off against a patient's age, AGE content can indicate diabetes mellitus in an early stage, so that early treatment of diabetes mellitus may be initiated in a large number of cases that would otherwise have been left undiagnosed.

The feature of claims 62 and 66 that the measured fluorescence is received from a small portion of the irradiated skin surface only is also advantageous for accurate measurement of autofluorescence. By providing that the measured fluorescence is received from an area of which the boundaries lie at least partially in the irradiated surface area of the skin, the measurement result becomes less influenced by differences from person to person in the optical properties of the skin with respect to absorption and scattering of light because boundary effects

occurring at the edges of the irradiated area (where less scattered light arrives than more centrally in the irradiated area) are avoided.

Of the cited prior art, only Talmor '181 provides for receiving fluorescence from a spot of an irradiated area only. However, firstly, Talmor '181 relates to measurement of fluorescence of a chemical that has been applied to a patient so as to determine to what extent it has been affected by local exposure to light, whereas claims 62 and 66 relate to measurement of the patient typical autofluorescence of clinically healthy skin. The skilled person would not expect to find a solution to problems associated to the measurement of the patient typical autofluorescence of clinically healthy skin in a document relating to the determination of the effect local exposure to light has had on photosensitive chemicals. Secondly, in Talmor '181, the purpose of the measurement of the fluorescence is to determine where high concentrations of a chemical having fluorescent properties are present. This requires a reasonable resolution, which does in turn require that the measurement spot is relatively small (see e.g. Talmor '181, col. 5, l. 49 - col. 6, l. 31). Such considerations are not applicable to the measurement of the autofluorescence of clinically healthy skin, where the purpose is not to map where fluorescence is high or low, but where a possibly very low level of autofluorescence typical for the patient is to be determined very accurately. Accordingly, the teaching of Talmor '181 would not have motivated the skilled person to provide the feature that the measured fluorescence is received from a small portion of the irradiated skin surface only for the determination of the autofluorescence of a clinically healthy skin.

For all the foregoing reasons, it is believed that all of the claims now present in this application are in condition for allowance, which is respectfully requested. If any further fees are required by this communication, please charge such fees to our Deposit Account No. 16-0820, Order No. VOB-34537US1.

Respectfully submitted,
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Date: 12-3-07